Whole-exome sequencing helpful to id gene mutations linked to nervous system diseases

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Use of exome sequencing improved the ability to identify the underlying gene mutations in patients with biochemically defined defects affecting multiple mitochondrial respiratory chain complexes (enzymes that are involved in basic energy production), according to a study in the July 2 issue of *JAMA*.

Defects of the mitochondrial respiratory chain have emerged as the most common cause of childhood and adult neurometabolic disease, with an estimated prevalence of l in 5,000 live births. Clinically these disorders can present at any time of life, are often seen in association with neurological impairment, and cause chronic disability and premature death. The diagnosis of mitochondrial disorders remains challenging, according to background information in the article. Examples of problems caused by mitochondrial diseases include a type of epilepsy; mitochondrial encephalopathy; lactic acidosis; and a syndrome that includes stroke-like episodes.

Robert W. Taylor, Ph.D., F.R.C.Path., of Newcastle University, Newcastle upon Tyne, U.K., and colleagues studied whether a whole-exome sequencing approach could help define the molecular basis of mitochondrial disease. Whole-exome sequencing is a complex laboratory process that determines the entire unique sequence of an organism's exome (the collection of exons, which are relatively small lengths of a whole genome and contain instructions for the body to build proteins).

The study included 53 patients, referred to 2 national centers in the

United Kingdom and Germany between 2005 and 2012, who had biochemical evidence of multiple respiratory chain complex defects. The majority (51/53 [96 percent]) of the patients presented during childhood (